

Letter to the Editor

Letter to the Editor concerning “Emdogain[®] in carcinogenesis: a systematic review of *in vitro* studies” by Laaksonen M, Sorsa T, Salo T (2010) *J Oral Sci* 52, 1-11

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Our recent review contained some inaccurate terms and formulations that may have caused unintended misinterpretations by scientists as well as clinicians. Oral carcinoma is rarely encountered and the combination of oral carcinoma with periodontitis is extremely rare. The implications of our review were meant to be limited to only those very few cases. Furthermore, the limitations of *in vitro* studies should have been more emphasized. Most of the malignant cell line investigations included in the review were of cells that were different to those found in the oral tissues and thus not relevant for clinicians. The available evidence for subsequent carcinogenic effects in oral malignant cell lines by enamel matrix derivative (EMD) is actually very weak. Thus, any generalizations that Emdogain[®] could cause cancer in any normal tissues, or in its normal indications, were not intended and may not be inferred from our *in vitro* study. A more appropriate title stating that this was a review of *in vitro* investigations with enamel matrix derivative using malignant cell lines would have clarified this.

Potential confusions may also have arisen from the use of Emdogain[®] and EMD as referring to the same material; EMD refers only to the protein isolate part of the material, whereas Emdogain[®] refers to the commercial product,

i.e. enamel matrix derivative 30 mg/ml and propylene glycol alginate (PGA) in an aqueous solution. In our review, EMD should only have been used to refer to enamel matrix derivative, not to the commercial product. Confusion in study reagents may result in bias, since it has been suggested that the PGA carrier may modify the bioactive properties of EMD (1). These errors in the abbreviation ‘EMD’ are frequent also in other studies and scientists should be more precise when talking about enamel matrix proteins.

The rationale for a hypothesis that EMD may be capable of inducing alterations in mucosal malignant tissues arose from a single case of a patient with existing dysplastic mucosal lesions treated with Emdogain. Due to constraints, it was only possible to include in our review very limited information concerning this case. One year after the carcinoma resection, a dysplastic verrucosus leukoplakia was observed on the anterior maxilla at the region of d.11. Three and a half years later a verrucosus leukoplakia appeared at the buccal region of d.47. The diagnosis was then again squamous cell carcinoma. Based on the follow-up history, it is highly possible that this patient had genetic susceptibility to dysplastic transition (‘field cancerization’), since recurrences of mucous dysplastic and cancer lesions have occurred several times during the recent past. Because of these limitations, this case cannot prove or even imply any causal role of Emdogain[®] treatment on the development of oral dysplastic changes or carcinoma. Thus, the weak level of clinical and *in vitro* evidence for carcinogenic effects of EMD does not warrant clinical recommendations and more *in vivo* and clinical evidence is required.

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